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Surgical Treatment of Middle Aortic Syndrome with Takayasu Arteritis or Midaortic Dysplastic Syndrome

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WHAT THIS PAPER ADDS

This study demonstrates the safety and excellent long-term durability of surgical treatment for middle aortic syndrome. Previous reports mostly dealt with congenital cases or stenosis in the thoracic aorta with little known about stenosis in the abdominal aorta caused by inflammatory arteritis. This study provides the anatomic and clinical characteristics, various operative methods for middle aortic syndrome caused by Takayasu arteritis, and emphasizes the need for long-term follow up.

Objective: Middle aortic syndrome (MAS) is a rare condition characterized by severe stenosis of the distal thoracic or abdominal aorta. The aims of this study are to define the anatomic characteristics of MAS and to review the various surgical methods and their outcomes in terms of long-term durability

Materials and methods: Ten adult patients were diagnosed with MAS caused by Takayasu arteritis (TA) or midaortic dysplastic syndrome and underwent surgical treatment between July 1992 and January 2013.

Result: The aortic lesions were mostly suprarenal ($n = 7$) and stenoses were commonly found in the celiac axis ($n = 6$), SMA ($n = 7$), and renal artery ($n = 6$). Indications for operation were uncontrolled hypertension in six patients and lower extremity claudication in four. Eight aortic bypasses, one supraceliac aortic interposition graft, and one bilateral aorto-renal bypass were performed. Adjunctive renal bypass with saphenous vein graft ($n = 4$) and IMA reimplantation ($n = 2$) were performed simultaneously. There was no post-operative mortality, and one complication of iliac dissection at the distal anastomosis site was detected and treated by stenting. Hypertension was cured or improved in five of the six patients, and lower extremity claudication improved in all of them. With a median follow up of 60 months (range, 12–263), all the aortic bypasses were patent and one adjunctive renal artery bypass graft with aortic bypass was occluded 29 months post-operatively.

Conclusions: Aortic bypass for MAS is safe and shows excellent long-term durability. Considering the patients are relatively young with a long life expectancy, aggressive surgical treatment could be beneficial. Lifelong follow up to monitor complications and disease progression is necessary.

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INTRODUCTION

Middle aortic syndrome (MAS) is a rare disease characterized by stenosis of the distal thoracic or abdominal aorta.[1–3] The renal and visceral arteries are commonly involved in MAS.[4] The etiologies are diverse, including congenital developmental anomaly, inflammatory aortitis, neurofibromatosis, and Williams syndrome. Takayasu arteritis is one of the most common causes of MAS in adults.[5,6] The most common symptoms of MAS are uncontrolled hypertension or arterial insufficiency distal to the stenosis, including lower extremity claudication.

There are several surgical treatment methods for MAS including thoraco-abdominal bypass, interposition aortic graft, and patch angioplasty. The general status and age of the patients, the exact location and extent of aortic lesion, and the existence of aortic branch disease should be considered when selecting the surgical technique. Recently, the outcomes of endovascular treatment, such as angioplasty or stenting, have been reported; however, long-term results are still lacking.[2,7,8]

Coarctation of the thoracic aorta is well recognized; however, little is known about stenosis in the abdominal

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aorta.[5] In addition, most of the reports about MAS have dealt with congenital cases in children. There are only a few reports of MAS in adults with other etiologies.

Here 10 adult patients, who were diagnosed with MAS mainly caused by Takayasu arteritis (TA) and underwent surgical treatment, are presented. The aims of this study are to define the anatomic characteristics of MAS and to review the various surgical methods and their outcomes in terms of long-term durability.

METHODS

Patients

Ten patients were diagnosed with MAS and underwent surgical treatment between 1992 and 2012. MAS was diagnosed by its characteristic radiological features: stenosis or occlusion in the distal thoracic or abdominal aorta on aortography or CT angiography. The clinical presentation, pre-operative radiological findings, operative methods, and follow up data were collected by a retrospective review of the medical records. An earlier publication from 1995 included four patients in this series.[9] This study was approved by the institutional review board of the Seoul National University Hospital.

Table 1. Baseline patient and anatomic characteristics.

Baseline patient characteristics	
Age at operation, years (median, range)	49 (23—59)
Age at diagnosis, years (median, range)	31 (8—50)
Sex (female)	8 (80%)
Clinical manifestations	
Renovascular hypertension	6 (60%)
Combined renal insufficiency	2 (20%)
Lower extremity claudication	4 (40%)
Other vascular lesions	
Cardiovascular	4 (40%)
Carotid artery or subclavian artery	6 (60%)
Inflammatory markers	
C-reactive protein, mg/dL (range)	0.12 (0.11—1.98)
Medical therapy at operation	
Corticosteroid	1 (10%)
Immunosuppression	1 (10%)
Anatomic characteristics	
Aortic disease	
Suprarenal	7 (70%)
Interrenal	1 (10%)
Infrarenal	2 (20%)
Aortic branch disease	
Renal artery	6 (60%)
Bilateral	4 (40%)
Unilateral	2 (20%)
Celiac axis	6 (60%)

Pre-operative imaging

Pre-operative imaging of the aorta and aortic branches, including the celiac axis, superior mesenteric artery (SMA), inferior mesenteric artery (IMA), and renal arteries, was done in all patients. Four patients from the earlier period of this study were investigated by conventional catheter-based aortography and recently all patients were examined with multi-slice thin section CT angiography. The aortic lesions were divided into three categories: suprarenal, interrenal, and infrarenal stenoses. Stenosis above the celiac artery or SMA is classified as “suprarenal,” stenosis below the SMA and between the renal arteries as “interrenal,” and stenosis below the renal artery as “infrarenal.”[1]

Operative technique

A subcostal incision in the ninth interspace was made for patients who required a thoraco-abdominal approach. A midline transperitoneal approach was used for the patients who underwent surgery for the abdominal aorta alone. The preferred conduit was the knitted Dacron for aortic bypass and autologous saphenous vein for renal bypass.

Histologic examination

Pathological examination of the tissues obtained during the operation was performed for five of the 10 patients. The pathological criteria of TA included arterial wall infiltration by lymphocytes, epithelioid cells or giant cells, destruction of medial elastic fibers, or replacement of medial smooth muscle cells by fibrosis.[10]

Clinical outcomes

The major clinical manifestations were uncontrolled hypertension and lower extremity claudication. In patients with refractory hypertension, the outcomes of hypertension control after the operation were classified as “cured” if the patients were normotensive without taking antihypertensive medication, “improved” if they were normotensive while on one or two medications, and “failed” if they were still hypertensive or required more than three medications. Improvements in claudication were assessed by symptoms and the ankle brachial index (ABI). When stenoses in the renal arteries were combined, the renal function was evaluated with the estimated GFR, which was calculated by the modification of diet in renal disease (MDRD) study equation.

Post-operative follow up

The patency of revascularization was assessed by angiography in the earlier period of the study and by CT angiography more recently. CT angiography was scheduled at 1, 6, and 12 months after the operation and annually thereafter. Blood pressure was measured at each visit, and ABI was checked annually. All patients were treated with one or two antiplatelet agents. Patients with active disease of inflammation were treated with corticosteroid or immunosuppressive agents.

Statistical analysis

Continuous data were summarized as the median with the range, and categorical data were summarized as proportions and percentages.

RESULTS

Patient characteristics

Eight female and two male patients were included. The median age at diagnosis of MAS was 31 (range 8—50) years and the median age at operation was 49 (range 23—59) years (Table 1). In seven of the 10 patients, TA was confirmed according to the American College of Rheumatology Diagnostic Criteria.[11,12] In the remaining three patients, the diagnosis could not be confirmed because they did not match the criteria or show the characteristic findings in the tissue samples. These three cases were highly indicative of sequelae of inflammatory vasculitis, and were considered to be midaortic dysplastic syndrome.

Clinical manifestations

Uncontrolled hypertension was a major clinical manifestation in six patients, whose median pre-operative systolic and diastolic blood pressure were 162 (range 132—190) and 87 (range 82—130) mmHg, respectively. All were treated with more than four antihypertensive medications. Renal insufficiency was combined in two patients, and their pre-operative estimated GFRs were 16.1 and 17.0 mL/min/1.73 m^2, respectively. Four patients presented with symptoms of lower extremity claudication, and the median pre-operative ABI was 0.49/0.44 (range, 0.45—1.08/0.44—1.08). Four patients had cardiac lesions, one had aortic regurgitation requiring valve replacement and three had congestive heart failure. Six patients had subclavian or carotid artery stenosis or occlusion. The median pre-operative C-reactive protein level (CRP) was 0.12 mg/dL (range 0.11—1.98). Two patients were treated with immunosuppressants, such as prednisolone or methotrexate, at the time of the operation.

Anatomic characteristics

The aortic lesion was suprarenal in eight patients (80%), interrenal in one (10%), and infrarenal in one (10%). As for aortic branch disease, renal artery stenosis was bilateral in four patients (40%) and unilateral in two (20%). Celiac axis stenosis or occlusion was found in six patients (60%) and a superior mesentery artery (SMA) lesion was identified in seven (70%).

Surgical techniques

An aorto-aortic bypass was performed in eight of 10 patients, with inflow from the distal thoracic aorta in five, the supraceliac aorta in one, and the infrarenal aorta in two patients. Knitted Dacron was used as the conduit in all aortic bypasses. In four of eight patients, simultaneous unilateral aorto-renal bypass with autologous saphenous vein was performed. In two of eight patients, re-implantation of the IMA to the aortic bypass graft was required. Because of severe stenosis in the celiac axis and SMA, abundant collaterals from the IMA supplied the small bowel, and reimplantation of it was required. An interposition aortic-aortic graft with knitted Dacron was performed in one patient with segmental stenosis in supraceliac aorta. Retrograde bilateral aorto-renal bypass with saphenous vein grafts was performed in one patient with severe stenosis in the both renal arteries (Fig. 1A,B).

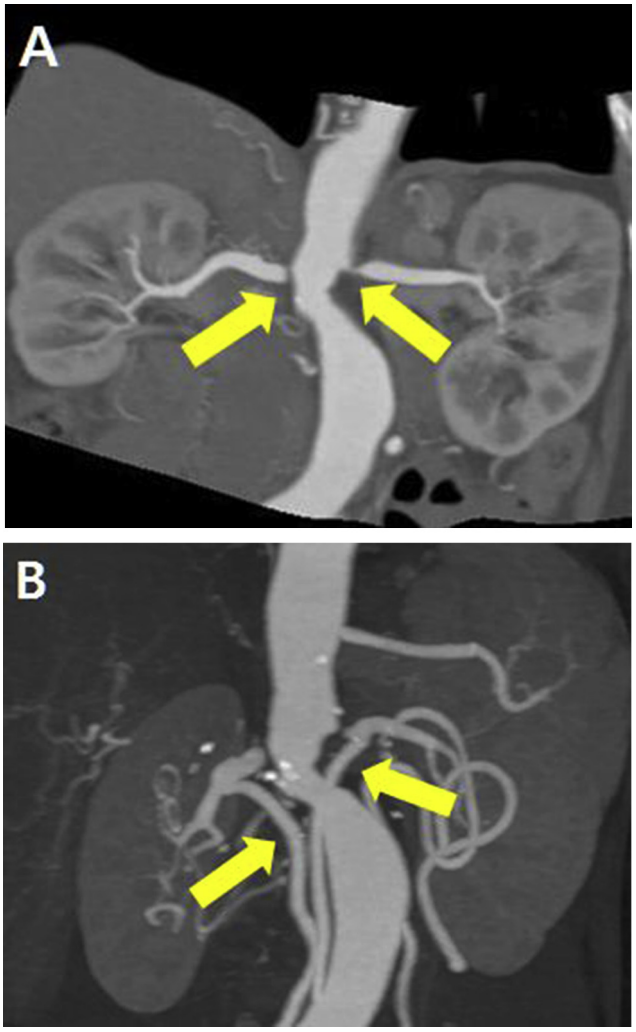

Figure 1. (A) Interrenal aortic coarctation. Pre-operative computed tomographic angiography (CTA) showed severe stenosis of bilateral renal arteries. (B) Bilateral retrograde aorto-renal bypass with reversed saphenous vein graft was performed successfully.

Operative outcomes

The median operative time was 337 minutes (range 220—565). When the patients were divided according to the site of inflow, the median operative time for the patients with inflow from the descending thoracic aorta was 500 minutes (range 220—595) and for patients with the abdominal aorta 214 minutes (range 285—250). The median length of hospital stay was 12 days (range 8—23). There was no post-operative mortality. One post-operative complication occurred in a 31 year old female with lower extremity claudication (Table 2, patient no. 8). Diffuse stenoses in the abdominal aorta, celiac axis, and right renal artery, and diffuse bilateral iliac hypoplasia were found on the pre-operative CT angiography (Fig. 2A). The patient underwent

bypass from the supraceliac aorta to the distal abdominal aorta with a Dacron graft (Fig. 2B,C). She developed right leg discomfort 5 days after the operation, and CT angiography revealed bilateral common iliac artery dissection from the distal anastomosis sites. She was treated by bilateral common iliac artery stenting (Fig. 2D).

With a median follow up of 60 months (range 12—263), all aortic bypass or interposition grafts were patent. One adjunctive aorto-renal graft with saphenous vein occluded and led to nephrectomy 29 months after the initial operation (Table 2, patient no. 4). No patient died during follow up; however, two patients were lost to follow up at 45 and 60 months respectively. One patient had progressive disease requiring additional endovascular treatment. At first, she underwent an aortic bypass with a Dacron graft for claudication and then required stenting of the right renal artery because of hypertension 27 months after the initial operation (Table 2, patient no. 8).

Clinical outcomes

Hypertension was cured in two, improved in three, and unchanged in one patient of the six with uncontrolled hypertension. The median systolic and diastolic blood pressures of all the patients at the last follow up were 117 (range 107—177) and 70 mmHg (range 54—82) respectively. One patient with unchanged hypertension (Table 2, patient no. 1) had diffuse stenosis in the abdominal aorta and left renal artery and total occlusion of the right renal artery on the pre-operative aortography. She underwent an aortic bypass from the descending thoracic aorta to aortic bifurcation with an 18 mm Dacron graft and a left aorto-renal bypass with a saphenous vein graft. Even though her renal bypass graft remained patent, she still required four types of antihypertensive medication: amlodipine, bisoprolol, candesartan, and hydralazine for blood pressure control. All patients with symptoms of claudication experienced complete relief of symptoms following bypass surgery. The median post-operative ABI was 1.05/1.00 (range 0.92—1.08/0.92—1.08).

DISCUSSION

Coarctation of the abdominal aorta is a rare disease caused by many different etiologies: TA, fibromuscular dysplasia, and developmental anomaly.[1] TA is chronic large vessel granulomatous arteritis that affects the aorta and its major branches.[13] The current study focused on patients with TA and excluded cases with developmental anomalies or atherosclerosis. The symptoms of MAS were secondary hypertension due to coarctation of the aorta, renal artery stenosis or increased systemic resistance, and arterial insufficiency in the lower extremities.[14] Surgical treatment is required to reduce the symptoms, to increase the quality of life, and ultimately to increase life expectancy.

There are several studies reporting the surgical experience of MAS caused by TA[10,13—18] (Table 3). Taketani et al.[14] analyzed 33 patients with TA and reported that overall and event-free survival rates at 20 years were 62.3% and 58.4%, respectively. Field et al.[10] showed that surgery for selected patients was safe and had excellent long-term results; however, patients with active disease were more likely to require revision. Previous reports mainly dealt with progression of the disease or survival and included all of the arterial areas. This study focused on abdominal aortic stenotic disease with many etiologies including Takayasu arteritis, and analyzed the surgical methods and clinical outcomes specifically.

Methods for aortic reconstruction include thoracoabdominal bypasses, interposition graft, and patch

Table 2. Summary of patients, methods, and operative results.

No	Age/Sex	Clinical manifestation	Aortic lesion	Aortic branch lesion	Name of operation	Concomitant procedures	Graft patency	Clinical outcomes	FU (mo)
1	23/F	Hypertension	Suprarenal	Celiac a., SMA, renal a.	Aortic bypass (DTA-bifurcation)	Lt renal a. bypass	Patent	Failed	263
2	45/F	Hypertension	Suprarenal	None	Aortic interposition graft	None	Patent	Cured	240
3	49/M	Hypertension	Suprarenal	SMA, Renal a.	Aortic bypass (DTA-bifurcation)	Lt renal a. bypass	Patent	Improved	214
4	50/M	Hypertension	Suprarenal	Renal a.	Aortic bypass (DTA-bifurcation)	Rt renal a. bypass	Renal bypass occlusion	Cured	45
5	59/F	Claudication	Infrarenal	Celiac a., SMA	Aortic bypass (Infrarenal-femoral a.)	IMA reimplantation	Patent	Cured	60
6	54/F	Claudication	Suprarenal	Celiac a., SMA	Aortic bypass (DTA-bifurcation)	IMA reimplantation	Patent	Cured	53
7	56/F	Hypertension	Suprarenal	Celiac a., SMA, renal a.	Aortic bypass (DTA-bifurcation)	Lt renal a. bypass	Patent	Improved	68
8	33/F	Claudication	Suprarenal	Celiac a., SMA, renal a.	Aortic bypass (Supraceliac-bifurcation)	None	Patent	Cured	54
9	49/F	Hypertension	Interrenal	Celiac a., SMA, renal a.	Aorto-renal bypass	None	Patent	Improved	23
10	56/F	Claudication	Infrarenal	None	Aortic bypass (Infrarenal-Iliac a.)	None	Patent	Cured	12

DTA = descending thoracic aorta; SMA = superior mesentery artery.

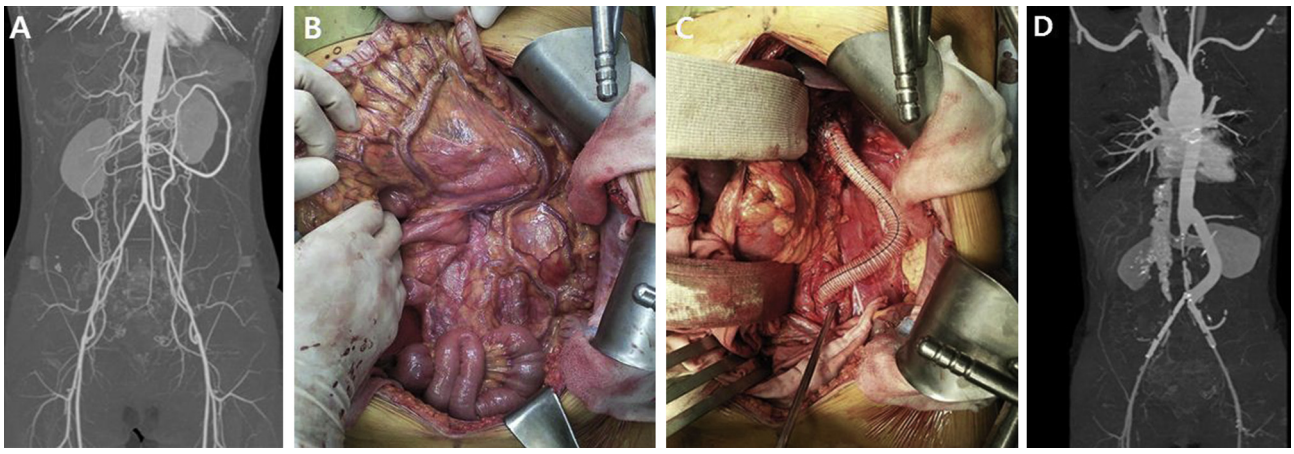

Figure 2. (A) Takayasu arteritis with claudication. Pre-operative CTA showed diffuse stenoses in the abdominal aorta, celiac axis, and right renal artery, and diffuse bilateral iliac artery hypoplasia. (B) Abundant collaterals from the IMA due to the stenotic celiac axis and SMA. (C) Bypass from the supraceliac aorta to the distal abdominal aorta with Dacron graft (D) Post-operative bilateral common iliac artery dissection from the distal anastomosis site was found and treated by stenting.

aortoplasty. Endovascular therapy can be a treatment option for MAS.[7,13,19] Even though there have been many reports of technically successful endovascular stenting for aortic coarctation, reports of long-term results and clinical improvements are sparse. Destruction of the elastic fibers in media and fibrosis of the adventitia could contribute to the poor response of the vessels to angioplasty in TA patients.[20] In addition, because of the high frequency of concomitant aortic branch disease, suitable cases for endovascular treatment are limited. In addition, the possibility of later conversion to surgical treatment should be considered. Considering that the patients are relatively young, long-term durability is one of the most important things when selecting the method of treatment. Therefore, the use of endovascular therapy should be prudent and reserved for patients with a focal aortic stenotic lesion or with high peri-operative risk.

There were neither post-operative deaths nor major complications in this series. The most common complication after surgery was cardiovascular or cerebrovascular disease associated with TA. No patient experienced stroke or heart failure peri-operatively. Even though aortic bypass in TA patients seems to be an aggressive procedure, it can be performed safely with a thorough pre-operative evaluation and proper patient selection. There was a report that stroke accounted for 9.5% of deaths in TA patients.[16] Miyata et al.[17] reported that the most common cause of death was congestive heart failure and the overall survival rate at 20 years after surgical treatment was 73.5%. A median follow up of 60 months is relatively short to determine late complications or death. Therefore, consistent follow up of these patients is required in terms of cardiovascular or cerebrovascular disease.

Dissection in the iliac arteries after clamping occurred in one patient. Fortunately, the dissection was found early and treated successfully by stenting. Thickened intima and fibrotic adventitia in TA patients can be the cause of arterial dissection. Another common surgical complication is anastomotic aneurysm. Destruction of the elastic component of the media, which occurs before fibrosis of the adventitia, can weaken the vessel wall and cause aneurysm.[21] According to a previous report, the incidence of anastomotic aneurysm was 13.8% at 20 years.[17] Another study reported the cumulative incidence of anastomotic aneurysm of 12.2% at 10 years, 21.2% at 20 years, and 37.3% at 30 years.[14] Most were detected incidentally without any symptoms or signs, and devastating results can happen unexpectedly. In a recent multicenter study with 166 vascular procedures in TA patients, the overall 5 and 10 year arterial complication free survival rates were only 56% and 45%, respectively.[18] In a series with 40 patients with TA, progression or recurrence of disease occurred in 40% of the patients over a mean follow up of 6.4 years.[15] Therefore, even though the present results look favorable with no anastomotic aneurysms, regular follow up using imaging modalities for arterial complications are necessary.

There was a patient who had sustained hypertension even after the operation. The 23 year old patient had had renovascular hypertension for 15 years and underwent aortic bypass with left renal artery bypass. She continued treatment with four kinds of antihypertensive medications, even though the bypass grafts were patent. Renal artery stenosis is a significant cause of hypertension in TA patients; however, hypertension occurs in 5—30% patients in the absence of renal artery stenosis.[21] Aortic coarctation, reduced aortic compliance, and dysfunction of the carotid baroreceptor could be the causes of hypertension in these patients. In the case of long-lasting renovascular hypertension or renal artery thrombosis, fundamental loss of renal parenchyma occurred and revascularization could not improve the clinical findings. Thorough evaluation of the arterial system and determination of which blood vessel is the main cause of the hypertension are required.

Aortic bypass or interposition was performed with the trans-abdominal approach without thoracotomy in four patients. Of these, two patients had a suprarenal lesion. Even though the aortic stenoses were diffusely involved

Table 3. Summary of reported cases of surgically treated Takayasu arteritis.

First Author	Year	Patients (n)	Arterial lesions (n)	Anatomic involvement (n)				Treatment		Outcomes	
				Aorta	Supra-aortic	Mesentery	Others	Surgery	Endovascular procedures	Postop. death	Event-free survival (%, median FU) Surgery Endovascular
Miyata[17]	2003	106	155	61	40	48	6	155	0	12	86.2% (20-year)[a]
Taketani[14]	2005	33	33	33	0	0	0	33	0	4	58.4% (20-year)
Fields[10]	2006	42	60	Not described				60	0	0	78.6% (5 year)
Ham[15]	2011	40	64	Not described				60	4	1	60% (6.4-year)
Kim[16]	2012	21	39	0	39	0	0	15	10	0	87.5%/46.7% (23.2 months)
Perera[13]	2012	37	64	Not described				33	31	0	79%/52% (6-year)
Saadoun[18]	2012	79	166	31	49	40	46	104	62	4	56% (5 year)

[a] Only for the incidence of anastomotic aneurysm.

from the supraceliac or suprarenal aorta, proximal control on the thoracic aorta is not always necessary. If there is enough space for aortic clamping and anastomosis to the non-diseased aorta, a trans-abdominal approach with medial visceral rotation could be an option to reduce the operative time and complications which follow thoracotomy. The patients with the trans-abdominal approach were followed up for 240 and 54 months after the operation respectively, and there was no problem at the anastomosis site or progression of aortic stenosis.

In this series, only two of the 10 patients were treated with steroids or immunosuppression: one with prednisolone (5 mg once a day) and methotrexate (7.5 mg once a week), and the other with prednisolone (10 mg once a day). Both patients have stable disease with normal CRP and ESR level. The patients who were referred to vascular surgeons were usually in a chronic state and on steroid therapy during the acute phase. It is recommended that revascularization procedures should not be performed during the active phase of the disease.[22] However, a uniform marker for disease activity is lacking and the serum marker does not always correlate with the inflammatory activity in the vessel wall.[10] Disease activity was assessed by combining clinical information, biomarkers, and image modalities.

Whether steroids or immunosuppression can prevent disease progression or recurrence after revascularization has been controversial. There were studies that showed freedom free revision, recurrence, or disease progression were not different between groups whether taking long-term steroids or not.[10,15] Park et al.,[23] however, reported a lower restenosis rate with post-interventional immunosuppressive treatment. In contrast with the conflicting results for immunosuppression, antiplatelet agents are recommended to prevent arterial ischemic events in TA patients.[24]

There are several limitations of this study. First, it is a retrospective case series with a small number of patients. Second, it reported the results of surgical bypass only and did not show comparative data with endovascular treatment. It is necessary to define the indications, technical aspects, and long-term outcomes of endovascular treatment in further studies.

CONCLUSION

MAS caused by TA or midaortic dysplastic syndrome presented in various locations of the aorta and was mostly combined with stenosis in the celiac axis, SMA, and renal arteries. Aortic bypass with concomitant renal bypass is safe and shows excellent long-term durability. Considering the patients are relatively young with long life expectancy, surgical treatment may be beneficial. Lifelong follow up is necessary to monitor for complications and disease progression.

CONFLICT OF INTEREST

None.

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